CHEMICAL PRODUCTS CORPORATION

CARTERSVILLE, GEORGIA 30120

POST OFFICE BOX 2470

TELEPHONE 770 · 382-2144
FAX 770 · 386-8053

October 29, 2002

Information Quality Guidelines Staff
Mail Code 28221T
U.S. EPA
1200 Pennsylvania Ave., N.W.
Washington, DC, 20460

Subject: Request for Correction of the IRIS Barium and Compounds substance file - Information disseminated by EPA that does not comply with EPA or OMB Information Quality Guidelines

Dear Madam or Sir;

Chemical Products Corporation (CPC), a Georgia corporation which produces Barium and Strontium chemicals at its Cartersville, Georgia facility, hereby submits this Request for Correction (RFC) concerning EPA's Integrated Risk Information System Barium and Compounds Substance File (IRIS Ba File). The influential information contained in this file fails to comply with the OMB "Guidelines for Ensuring and Maximizing the Quality, Objectivity, Utility, and Integrity of Information Disseminated by Federal Agencies".

The information disseminated in EPA's IRIS Barium and Compounds file directly contradicts the information published by EPA in the January 3, 1997 Federal Register and, therefore, cannot represent an EPA consensus position. The IRIS Ba File was revised in 1998 and 1999, yet it contains no mention of the toxicological evaluation conducted by EPA's Office of Pollution, Pesticides, and Toxic Substances reported in 62 FR 366-372 (No. 2, January 3, 1997). There is no explanation of how a radically different interpretation of the same data could be justified. The NOAEL employed to

calculate the Oral Reference Dose in the IRIS Ba File is 0.21 mg/kg/day; there is no LOAEL associated with this NOAEL. The NOAEL reported in 62 FR 366-372 is 70 mg/kg/day in rats and 165 mg/kg/day in mice; these values are taken from a National Toxicology Program technical report and are associated with a LOAEL of 180 mg/kg/day. EPA's Technical Summary in 62 FR 366-372 states, "the data from animal studies support a LOAEL of approximately 180 mg/kg/day for renal toxicity." The IRIS Ba File reports a LOAEL of 75 mg/kg/day based upon an insignificant effect reported in the same National Toxicology Program study. Accordingly, the IRIS Ba File cannot represent a consensus among EPA offices because the toxicological evaluation of Barium conducted by EPA's Office of Pollution, Pesticides, and Toxic Substances reported a different critical effect and a different LOAEL than the IRIS Ba File when evaluating the same studies.

CPC will submit information in this letter demonstrating that the IRIS Ba File is scientifically untenable. A Barium Oral Reference Dose derivation by University of Georgia toxicologists Cham Dallas and Phillip Williams has been funded by CPC. This document is consistent with the EPA's Office of Pollution, Pesticides, and Toxic Substances toxicological evaluation. CPC also funded face-to-face expert peer review of the Dallas and Williams document under the auspices of Toxicological Excellence in Risk Assessment (TERA). The Dallas and Williams derivation of an Oral Reference Dose for Barium and Compounds is enclosed with this letter. CPC requests that the information contained in the IRIS Barium and Compounds Substance File be corrected as soon as possible by replacing the existing IRIS Barium and Compounds substance file with the Dallas and Williams derivation of an Oral Reference Dose for Barium and Compounds.

CPC provides the following information as required by section 8.2 of EPA's Information Quality Guidelines:

- **Name and contact information for the individual or organization submitting a complaint; identification of an individual to serve as a contact.** This complaint is submitted by Chemical Products Corporation (CPC). The individual to serve as contact at Chemical Products Corporation is Jerry A. Cook, Technical Director. He can be contacted at Chemical Products Corporation, P.O. Box 2470, Cartersville, Georgia 30120-1692; telephone 770-382-2144, fax 770-386-6053, email JACook@CPC-Ga.com.

- **A description of the information the person believes does not comply with EPA or OMB guidelines, including specific citations to the information and to the EPA or OMB guidelines, if applicable.** The Oral Reference Dose for Barium derived in the Barium and Compounds Substance File in EPA's Integrated Risk Information System, as well as the presentation and analysis of the supporting data, do not comply with the OMB requirements for objectivity or for reproducibility. The Office of Management and Budget's "Guidelines for Ensuring and Maximizing the Quality, Objectivity, Utility, and Integrity of Information Disseminated by Federal Agencies" requires information disseminated by Federal Agencies to be objective, that is "being presented in an accurate, clear, complete, and unbiased manner, and as a matter of substance, is accurate, reliable, and unbiased." (67 FR 8451-8460). These guidelines also require information disseminated by Federal Agencies to be reproducible; 67 FR 8451-8460 states, "'Reproducibility' means that the information is capable of being substantially reproduced, subject to an acceptable degree of imprecision. For information judged to have more (less) important impacts, the degree of imprecision that is tolerated is reduced (increased). If agencies apply the reproducibility test to specific types of original or supporting data, the associated guidelines shall provide relevant definitions of reproducibility (e.g., standards for replication of laboratory data). With respect to analytic results, 'capable of being substantially reproduced' means that independent analysis of the original or supporting data using identical methods would generate similar analytic results, subject to an acceptable degree of imprecision or

error." **OMB calls specific attention to this requirement,** "We also want to build on a general observation that we made in our final guidelines published in September 2001. In those guidelines we stated: '... in those situations involving influential scientific[, financial,] or statistical information, the substantial reproducibility standard is added as a quality standard above and beyond some peer review quality standards' (66 FR 49722 (September 28, 2001))."

CPC requests that EPA withdraw the March 30, 1998 IRIS file revision for barium (with minor subsequent revisions) and replace it with the "Determination of the Oral Reference Dose (RfD) for Barium and Compounds (CAS No. 7440-39-3) with Supporting Documentation" authored by Dallas and Williams which has been subjected to independent peer review under the auspices of Toxicological Excellence in Risk Assessment (TERA), a nonprofit corporation located in Cincinnati, Ohio.

- **An explanation of how the information does not comply with EPA or OMB guidelines and a recommendation of corrective action. EPA considers that the complainant has the burden of demonstrating that the information does not comply with EPA or OMB guidelines and that a particular corrective action would be appropriate.** EPA incorrectly identified hypertension as the critical effect for chronic barium toxicity in its IRIS Ba File. The Oral Reference Dose in the IRIS Ba File is derived from a human study in which volunteers were administered low doses of soluble barium for short periods of time and then evaluated for cardiovascular effects. No adverse effects were observed; the highest dose tested is inappropriately designated a NOAEL even though there is no LOAEL associated with this study. Identification of cardiovascular effects as the critical effect for chronic barium ingestion has been shown to be erroneous.

The Peer Review Record for the 1998 revision of the IRIS Ba File demonstrates that this work product did not undergo the requisite properly-conducted peer review. No peer review was conducted to support the editorial revisions made in 1999 which

included removing "Hypertension" from the "Critical Effect" column of the table at section I.A.1. and replacing it with "No Adverse Effect" in conjunction with a footnote to the table stating in part, "Previous investigations in research animals (both acute and chronic) have demonstrated the potential for hypertension to develop as a result of high barium exposures." This footnote is inaccurate. While acute, very high exposures have led to observed hypertension in both laboratory animals and humans, there is only one poorly designed and poorly conducted study, Perry et al. (Veterans' Administration Medical Center, St. Louis, MO), which reports hypertension as a chronic or sub-chronic effect in rats. This single study was reported, in whole or in part, five separate times between 1983 and 1989 without making any reference to earlier publication. The myriad problems with the Perry et al. study were detailed in a letter CPC sent to Administrator Carol Browner dated April 20, 1998, a copy of which is enclosed.

The EPA-funded Perry et al. study conveniently reported hypertension from chronic barium ingestion 8 years after EPA had promulgated a drinking water standard for soluble barium based upon hypothesized cardiovascular effects from low-level chronic barium ingestion ("Because of the seriousness of the toxic effects of barium on the heart, blood vessels, and nerves, drinking water shall not contain barium in a concentration exceeding 1 mg/l.", U.S. Environmental Protection Agency, Statement of Basis and Purpose for the National Interim Primary Drinking Water Regulations, PB-250 011, December 1975, 71-73).

A study reported by McCauley et al. (EPA's Health Effects Research Laboratory) at about the same time (1982) concluded, "There were no significant trends toward hypertension in any of the rats given as much as 1000 ppm Ba for 16 weeks." This refers to the highest dose tested by McCauley; this is 10 times higher than the dose reported by Perry et al. to cause hypertension in rats after only 4 weeks exposure. In fact, McCauley found that 1000 ppm soluble Ba prevented specially-bred salt-sensitive rats from developing salt-induced hypertension. The McCauley paper, at page 210, states,

"The research described in this article has been reviewed by the Health Effects Research Laboratory and approved for publication.". In spite of the well-conducted study by its own Health Effects Research Laboratory, EPA chose to adopt the grossly flawed Perry et al. study to use as a basis for its initial IRIS Oral Reference Dose for Barium in 1987; in this way the IRIS Oral RfD was made consistent with the already-existing drinking water MCL for soluble barium.

National Toxicology Program "Technical Report on the Toxicology and Carcinogenesis Studies of Barium Chloride Dihydrate (CAS no. 10326279) in F344/N rats and B6C3F1 mice (drinking water studies)" (NTP TR 432, NIH pub. no. 943163. NTIS pub PB94214178, 1994) found no blood pressure increase in rats after administration of up to 4000 ppm barium chloride dihydrate for 13 weeks in the drinking water; this is 40 times the dose reported by Perry et al. to cause hypertension in rats after only 4 weeks exposure. None of the physiological effects of hypertension were found after 2 years exposure to elevated levels of soluble barium in the drinking water. This NTP report states at page 52, ".... an association between barium and cardiovascular effects in the present studies does not seem to be likely....".

CPC detailed the gross inadequacies of the peer review of the 1998 IRIS work product in a letter to Assistant Administrator Norine Noonan dated March 5, 1999 and also in a letter to Deputy Administrator Peter Robertson dated March 12, 1999. A copy of CPC's March 5, 1999 letter to Assistant Administrator Noonan is enclosed herewith. Assistant Administrator Noonan responded in a letter dated April 21, 1999 stating, in part, "You were correct, however, that the charge to external peer reviewers was missing from the file. This was a filing oversight and the charge has been added. Enclosed is a copy of the charge for your use." A copy of a letter sent to prospective external reviewers by EPA's contractor, ERG Inc., was included with her letter; this general outline of contractual conditions and duties bears no resemblance to the example of a charge for IRIS peer reviewers which is included in the EPA's Peer

Review Handbook at page B-11 (for cumene which was reviewed in early 1997). The ERG letter which Dr. Noonan sent to us could not reasonably be called a charge, thus our statement that there is no charge included in the Peer Review Record for the IRIS Ba File is accurate.

The peer review conducted for the 1998 review and revision of the Barium and Compounds file in IRIS clearly does not meet the minimum standards required by EPA's Peer Review Handbook. However, even if the IRIS Barium and Compounds substance file had been properly peer reviewed, it fails to meet the reproducibility requirement found in the OMB Quality Guidelines at V.3.b.ii: "If an agency is responsible for disseminating influential scientific, financial, or statistical information, agency guidelines shall include a high degree of transparency about data and methods to facilitate the reproducibility of such information by qualified third parties. OMB believes that a reproducibility standard is practical and appropriate for information that is considered 'influential', as defined in paragraph V.9--that 'will have or does have a clear and substantial impact on important public policies or important private sector decisions.' The reproducibility standard applicable to influential scientific, financial, or statistical information is intended to ensure that information disseminated by agencies is sufficiently transparent in terms of data and methods of analysis that it would be feasible for a replication to be conducted. The fact that the use of original and supporting data and analytic results have been deemed 'defensible' by peer-review procedures does not necessarily imply that the results are transparent and replicable."

The results of the IRIS review and revision of the IRIS Ba File are not transparent and replicable. Three separate entities: EPA's Office of Pollution Prevention and Toxic Substances, independent University of Georgia toxicologists, and an expert face-to-face peer review panel all determined that the National Toxicology Program (NTP) study was the most appropriate study from which to derive an Oral Reference Dose for Barium; the IRIS Ba File bases its Oral Reference Dose on a very limited human study of short duration in which no adverse effects were found.

The IRIS Ba File's analysis of the NTP study is also not replicable. The IRIS Ba File derives LOAEL and NOAEL values from kidney weight differences. Kidney weights were measured at the 15 month interim evaluation in the 2 year rat study, but not measured by NTP at the conclusion of the 2 year study. Once again, EPA's Office of Pollution Prevention and Toxic Substances, independent University of Georgia toxicologists perparing an Oral Reference Dose determination, and an expert face-to-face peer review panel all concluded that the kidney weight changes were not significant and determined higher LOAEL and NOAEL values from their analysis of the NTP study. The IRIS Barium and Compounds substance file does not meet the requirements of OMB's reproducibility standard in such significant areas that it should be replaced in its entirety.

- **An explanation of how the alleged error affects or how a correction would benefit the requestor.** Revision of the IRIS Ba File to present a scientifically-sound (and substantially increased) Oral Reference Dose for Barium will allow CPC to pursue review and upward revision of EPA's Toxicity Characteristic regulatory level for soluble barium in wastes. EPA's Office of Solid Waste has been unwilling or unable to address the issue of a substantial change in the regulatory level for soluble barium under RCRA without a prior substantial increase in the Oral Reference Dose for Barium in IRIS.

The use of barium compounds in the United States has been adversely impacted by the low regulatory limit imposed on Barium-containing wastes by RCRA. CPC, a Georgia corporation which has been producing barium chemicals at its Cartersville, Georgia facility for almost 70 years, has been vigorously pursuing the goal of upward revision of the RCRA regulatory limit for barium to reflect sound science. All of the barium compound products produced by CPC exhibit sufficient solubility in the weak acetic acid leaching solution employed in EPA's Toxic Characteristic Leaching Procedure (TCLP) to exceed the present regulatory limit for barium under RCRA. Barium compounds that would be a hazardous waste based upon the characteristic of

soluble barium could be used by many small and medium-sized industrial concerns in the ceramics industry, the paint industry, and the plastics industry. CPC's sales of barium compounds to these industries have been limited by the concern of many potential customers that the miscellaneous waste they generate in the course of their everyday business activities could exceed the existing RCRA regulatory limit for soluble barium.

CPC believes that an upward revision of the IRIS Oral Reference Dose for Barium and Compounds is dictated by sound science. This would lead to a substantial increase in the RCRA regulatory limit for Barium, which would lead to a substantial increase in the use of CPC's barium compound products. We request that the scientifically-sound Dallas and Williams Oral Reference Dose Determination be placed into IRIS in place of the flawed existing IRIS Barium and Compounds Oral Reference Dose Determination.

If I can answer any questions concerning this RFC, or supply additional information, please telephone me at 770-382-2144.

Sincerely,

Jerry A. Cook

Technical Director

Enclosures:

CPC letter to Administrator Browner, April 20, 1998

CPC letter to Assistant Administrator Noonan, March 5, 1999

"Determination of the Oral Reference Dose .....", Dallas and Williams, January, 2000

November 15, 2002

Associate Director for Communications
Office of the Director
National Institutes of Health
Building 1, Room 344
9000 Rockville Pike
Bethesda, MD 20892

Subject: Submission of Information Quality Request For Correction - NTP Summary of Draft TR-494 at http://ntp-server.niehs.nih.gov/htdocs/LT-studies/tr494.html

Dear Madam or Sir;

This letter is an Information Quality Request For Correction submitted by Chemical Products Corporation (CPC), a Georgia corporation located in Cartersville, Georgia. CPC produces Anthraquinone aqueous suspensions for use by the North American paper industry as a catalyst in the Kraft pulping process. CPC's affiliate, Chemical Products Technologies, LLC markets these Anthraquinone aqueous suspensions to the North American paper industry.

CPC requests that the Abstract of Draft Technical Report TR-494, Toxicology and Carcinogenesis Studies of Anthraquinone (CAS No. 84-65-1) in F344/N Rats and B6C3F1 Mice (Feed Studies) be withdrawn from the NTP web site and all other locations where it is available to the public. We request that it be replaced with a statement explaining that a contaminant in the Anthraquinone sample tested by NTP confounded the results of the testing and that Draft TR-494 will be withdrawn, rewritten, and resubmitted for peer review.

Copies of three letters from Dr. Kenneth Olden to CPC are enclosed herewith. In response to information submitted to him by CPC, Dr. Olden initiated laboratory testing to determine the identity of an unidentified contaminant in the NTP Anthraquinone sample employed in the TR-494 studies, committed to conducting mutagenicity tests on pure Anthraquinone samples, and stated that the results of this further work would be incorporated into a rewritten TR-494.

CPC applauds Dr. Olden's obvious commitment to sound science at NTP. We are grateful that he was willing to objectively consider the information we supplied to him and that he took decisive action when he determined that action was warranted. In this regard, we believe that he is uniquely laudable. However, it has been more than 2 years since CPC received Dr. Olden's letters. During this time the Abstract of TR-494 on the NTP web site has not been modified to give the public any indication that there are highly significant unresolved issues concerning the conclusions of Draft TR-494.

We submit that the Abstract of Draft TR-494 is known to NTP to contain information which does not conform to the Guidelines for Ensuring the Quality of Information Disseminated to the Public.

The Anthraquinone sample tested in the long term NTP studies reported in Draft TR-494 contains a mutagenic contaminant which has rendered the Draft TR-494 report and the peer review of that Draft report invalid. The Draft TR-494 stated, "Anthraquinone was mutagenic in Salmonella typhimurium strains TA98 and TA100 with and without S9 metabolic activation enzymes." This statement was acknowledged by Dr. Kenneth Olden to be incorrect in his letter dated September 26, 2000 wherein he states, "We agree that there is still considerable uncertainty about the mutagenicity of anthraquinone". The peer review of Draft TR-494 was conducted based upon the incorrect assumption that Anthraquinone was conclusively known to be mutagenic. In fact, a preponderance of published data demonstrate that Anthraquinone is not a mutagen.

The following information about this Request For Correction is provided following the specific format outlined in the "Responsibility of the Complainant" section of the HHS Guidelines for Ensuring the Quality of Information Disseminated to the Public.

• A detailed description of the specific material that is proposed for correction, including where the material is located, i.e., the publication title, date, and publication number, if any, or the web site and web page address (URL), or the presentation, presenter, date and mode of delivery; - The material proposed for correction is the Abstract of Draft Technical Report TR-494 Toxicology and Carcinogenesis Studies of Anthraquinone (CAS No. 84-65-1) in F344/N Rats and B6C3F1 Mice (Feed Studies), Report date May 1999, NIH Publication Number 99-3953, found on the NTP web site under "long term studies" at http://ntp-server.niehs.nih.gov/htdocs/LT-studies/tr494.html, and possibly elsewhere within NTP.

• the specific reasons for believing that the information does not comply with OMB, HHS, or NIH guidelines and is in error, and supporting documentation, if any: - In reviewing all of the information available concerning Anthraquinone, including the Draft TR-494, CPC discovered important discrepancies between the statements in TR-494 and other published information. Specifically, many Anthraquinone samples had been tested for mutagenicity in Salmonella typhimurium and had been determined not to be mutagenic; this fact was not fully considered in TR-494.

CPC learned that NTP had not actually tested the Anthraquinone sample employed in TR-494 for mutagenicity. CPC obtained a portion of the Anthraquinone retained sample from NTP and submitted it to a respected independent laboratory for mutagenicity testing along with three other samples of Anthraquinone.

Of four samples of Anthraquinone submitted for testing, only the NTP TR-494 sample was mutagenic in Salmonella typhimurium strains TA98 and TA100. CPC submitted this information to Dr. Kenneth Olden along with information about the contents of EPA's TSCA file for Anthraquinone which describes a sample of

Anthraquinone found to be mutagenic; this sample was purified to remove trace nitroanthracene contamination and was found not to be mutagenic on retesting. In response to these submissions by CPC, Dr. Kenneth Olden acknowledged that the mutagenicity of pure Anthraquinone was in question.

• Suggested recommendations for what corrective action(s) should be taken: - CPC requests that the Abstract of Draft TR-494 be immediately withdrawn from the NTP web site and replaced with a statement that a mutagenic contaminant in the Anthraquinone sample tested by NTP was subsequently identified thus confounding the conclusions of the draft report and invalidating the peer review of Draft TR-494 conducted in May, 1999 before the presence of the contaminant became known.

• A description of how the person requesting the correction is affected by the information error: - CPC and Chemical Products Technologies, LLC are adversely affected by reduced sales of their Anthraquinone suspension product to the North American paper industry. We believe that the North American paper industry has been reluctant to realize the increased pulp recovery benefits of Anthraquinone use because of the conclusions of NTP Draft Report TR-494 and concern about possible adverse consequences of employing a catalyst in the Kraft pulping process which has been alleged to have carcinogenic activity in rats and mice.

• Complete contact information for the requester, including name, mailing address, telephone number, e-mail address, and organizational affiliation, if any, - This letter is submitted by Jerry A. Cook, Technical Director, Chemical Products Corporation, P.O. Box 2470, Cartersville, GA 30120-1692, telephone number 770-382-2144 extension 272, email JACook@CPC-Ga.com who is affiliated with Chemical Products Corporation and Chemical Products Technologies, LLC.

Sincerely,

Jerry A. Cook
Technical Director

Enclosures: Dr. Olden letter dated August 21, 2000
Dr. Olden letter dated September 26, 2000
Dr. Olden letter dated October 26, 2000

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Institute of
Environmental Health Sciences
P.O. Box 12233
Research Triangle Park, N.C. 27709

August 21, 2000

Mr. Jerry A. Cook
Technical Director
Chemical Products Corporation
Cartersville, Georgia 30120

Dear Mr. Cook:

Thank you for your letter of July 25 concerning Technical Report Number 494 on the Toxicology and Carcinogenesis Studies of Anthraquinone.

We are unaware of any factual errors in the draft of Technical Report Number 494; presumably you are referring to the 0.1% contaminant in the sample of anthraquinone used for this study, which was not identified at the time the study was conducted. However, to ensure that the report accurately reflects the test material that was evaluated, we are currently in the process of determining that the sample used in our studies did indeed contain one or more nitroanthracene isomers. The identity of the isomers is also being determined.

Since anthraquinone prepared by the oxidation of anthracene might contain nitroanthracene isomers as contaminants, the method used to manufacture the test sample is also being determined. Please be assured that the final version of Technical Report Number 494 will contain this information, and will discuss its potential impact on the interpretation of the results of the anthraquinone study.

Sincerely yours,

Ken Olden

Kenneth Olden, Ph.D.
Director

cc:
Dr. Richard Irwin

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Institute of
Environmental Health Sciences
P.O. Box 12233
Research Triangle Park, N.C. 27709

September 26, 2000

Mr. Jerry A. Cook
Technical Director
Chemical Products Corporation
Post Office Box 2470
Cartersville, Georgia 30120

Dear Mr. Cook:

Thank you for your letter of August 24 and for the information contained therein. We agree that there is still considerable uncertainty about the mutagenicity of anthraquinone, its metabolites and 9-nitroanthracene. We, therefore, are initiating a series of mutagenicity tests with these compounds using material which has been verified to be 100% pure.

Once again, let me assure you that the results of this testing will be included in the final version of Technical Report 494 along with a complete discussion of their impact on the interpretation of the results.

Sincerely yours,

Ken Olden

Kenneth Olden, Ph.D.
Director

cc:
Dr. Richard Irwin

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Institute of
Environmental Health Sciences
P.O. Box 12233
Research Triangle Park, N.C. 27709

October 26, 2000

Mr. Jerry A. Cook
Technical Director
Chemical Products Corporation
Post Office Box 2470
Cartersville, Georgia 30120

Dear Mr. Cook:

Thank you for the copy of the report from BioReliance on your most recent mutagenicity studies. As I stated in my previous letter, we have initiated a series of mutagenicity tests on anthraquinone and its metabolites. The results of these studies and other pertinent information on the purity of the anthraquinone sample used in our two-year study will be included in the final version of Technical Report 494 along with a discussion of the impact of this information on the interpretation of the two-year study.

Sincerely yours,

Ken Olden

Kenneth Olden, Ph.D.
Director

cc:
Dr. Richard Irwin